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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,725	02/04/2004	Christophe Alain Thuriéau	082/US/PCT2/US-A	4960

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EXAMINER
TUCKER, ZACHARY C

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 12/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,725	THURIEAU ET AL.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-20 and 30-36* is/are pending in the application.

4a) Of the above claim(s) *5-8,10,12-20 and 30-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☒ Claim(s) *9 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment

As requested by applicants, in the correspondence filed 10 October 2006 (hereinafter "present amendment"), which is in reply to the non-final action mailed 27 April 2006 (hereinafter "previous Office action"), claim 1 has been amended. The amendment to the specification, starting at page one, has also been entered as requested.

Election/Restrictions

Because the search of claim 1 has been broadened and continued, and prior art anticipating that claim once again found, the search has been stopped. Claim 1 has not been completely searched; claims 9 and 11 *have* been completely searched and are objected to, but would be allowable if amended to include all of the limitations of the base claim (which is claim 1).

Comments regarding the withdrawn method-of-treatment claims are provided in the latter part of this Office action, and in the following paragraph. Conditions required for rejoinder of claims 30-36 have not been met at this time; as the claims of the elected invention (the compounds *per se*) are not currently in allowable form.

Claim 30, drawn to the pharmaceutical composition, would not present any patentability issues upon its rejoinder. On the other hand, claims 31-36, drawn to methods of treating various medical conditions, disorders and diseases, and therapeutic methods of eliciting an agonist or antagonist effect at a somatostatin receptor subtype, and a method of "binding" one or more of a somatostatin receptor subtype in a subject in need thereof will present new patentability issues upon their rejoinder. The methods of treating the medical conditions, disorders and diseases are not completely enabled by the disclosure, notwithstanding the lengthy submission of references offered by applicants, ostensibly as evidence that they indeed *are* enabled (vide infra). Methods wherein an agonist or

antagonist effect is elicited from one or more somatostatin receptor subtypes, or the method wherein a somatostatin receptor subtype is "bound" *in a subject in need thereof*, are both indefinite under the second paragraph of 35 U.S.C. 112, and non-enabled under the first paragraph of that statute. Exactly which subjects are *in need of* somatostatin receptor agonism or antagonism is not clear and well-defined when the claims are read in light of the specification, because even though many diseases for which these pharmacological effects allegedly are effective treatments are taught in the specification, these are only offered as examples, thus the full scope of the claims drawn to eliciting an agonist or antagonist effect at a somatostatin receptor subtype is therefore not clear and well-defined. Which individuals are *in need of* somatostatin receptor subtype binding is further not clear and well-defined when the claim drawn to that method is read in light of the specification. What the result of simply "binding" the receptor is, as opposed to eliciting an agonist or antagonist effect is not understood. The mode of action claims are not compliant with the first paragraph of 35 U.S.C. 112, because the "how to use" portion of that paragraph of the statute is not met in full with respect to such claims. Only some exemplary modes of using such a method are provided in the specification. Additionally, mode of action claims would potentially cover methods of treating diseases which have yet to be identified by the physician of ordinary skill in the medical arts.

Because prior art anticipating claims which read on the elected species has again been found, claims *not* readable on the elected species, 5-8, 10 and 12-20, remain withdrawn from consideration. Applicants should take note that a reply after a Final Rejection which requires the examiner to again broaden and continue the search may be denied entry, as explained in MPEP 803.02. Similarly, as explained below in the section headed "Allowable Subject Matter," rejoinder of now withdrawn method of treatment claims which would present new patentability issues will prompt refusal to enter an

amendment after final which otherwise would place the claims of the elected group in condition for allowance.

Status of Double Patenting Rejection

In the previous Office action, claim 1 was rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 3 of US 6,852,725 (To Thurieau et al).

The terminal disclaimer filed on 10 October 2006, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of the patent, has been reviewed and is accepted. Thus, the double patenting rejection is hereby withdrawn.

Status of Claim Rejections - 35 USC § 102

In the previous Office action, claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by von Geldern et al, *Journal of Medicinal Chemistry*. Vol. 39(4), pages 957-967 (1996).

In view of the present amendment to claim 1, the rejection is hereby withdrawn. Claim 1 as amended specifically excludes from its scope the compound dubbed "8N" as reported in the von Geldern et al reference.

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New Claim Rejection - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The present amendment to claim 1, which amendment specifically excludes one single compound from the von Geldern et al reference, cited in the previous Office action in the rejection under 35 U.S.C. 102(b) of that claim, is new matter because applicants did not describe the compound indicated as "8N" in the von Geldern et al reference and now represented by a molecular structure diagram in claim 1's new proviso, in the disclosure and claims as originally filed. The exclusion of this compound from claim 1 introduces a new concept into the claim set insofar as all of the variables in formula (I) of claim 1 previously were variable *independently* of one another, and now, by virtue of the new proviso limitation, variables in formula (I) now are *interdependent* upon one another's identities in a complicated relationship. For example, now, by virtue of the present amendment, variable R^6 cannot be carboxy (-COOH) when R^5 is methyl; when R^1 is a proton, R^3 cannot be $-(CH_2)$-indol-3-yl, and so on. None of these new relationships between the variables in formula (I) were contemplated by the inventors at the time the invention was made (see MPEP 2173.05(i), second paragraph).

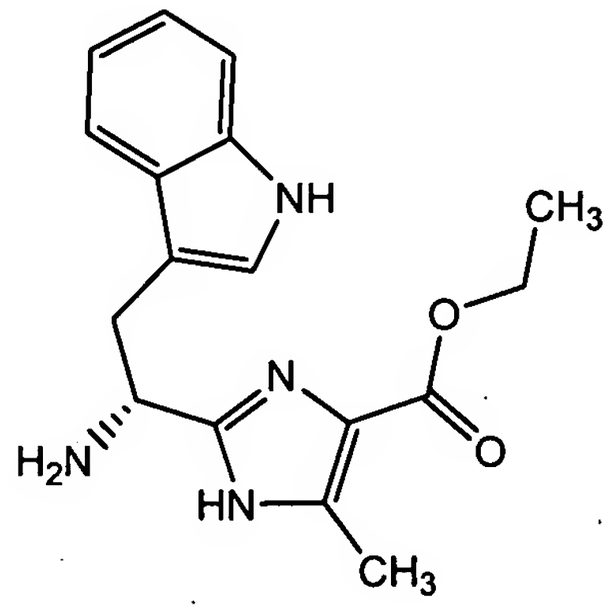
New Claim Rejection - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/08550 (von Geldern et al 1995).

At least one compound embraced by instant claim 1 is disclosed in the von Geldern et al 1995 publication. On page 51, Example 1C describes the synthesis of an intermediate compound, 2-[(R)-1-amino-2-(indol-3-yl)ethyl]-5-methyl-imidazole-4-carboxylic acid ethyl ester. This compound is embraced by instant claim 1 wherein R^1 is hydrogen; R^2

and R^4 are both hydrogen; R^3 is $-(CH_2)$-indol-3-yl; R^5 is $[(C_1\text{-}C_6)\text{alkyl}]_m\text{-}C(O)\text{-}O\text{-}Z^5$, wherein m=0 and Z^5 $(C_1\text{-}C_{12})$alkyl (methyl); R^6 is $(C_1\text{-}C_6)$alkyl (methyl). The compound is represented by the structure diagram below:



Specification

The present amendment is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

About three pages of material, starting at page one, line 20, have been added. This material consists of dozens of literature citations, ostensibly providing for guidance enabling the practice of the methods according to instant claims 31-36. What renders this material new matter, in particular, is that the activity of the compounds according to the invention has been set out as correlative with the results of these numerous citations from the medical and scientific literature. At the time the invention was made, applicants had not set the compounds of the invention out as having activity corresponding to or correlating with the results of the experiments reported in the various cited publications. Applicants had not taught in the specification as originally filed that compounds of the present invention were amenable to application in the manner suggested and described in these various publications. As such, the new material added to the instant specification

constitutes new matter. Note the third through fifth line of the paragraph added to the specification by virtue of the present amendment:

> "Thus, the administration of an imidazolyl derivative of this invention which binds selectively to somatostatin receptor subtypes can treat medical disorders which are mediated by somatostatin receptor subtypes. For example, for treating acromegaly, see, e.g., Robbins, R. J., ...

Each of the specific disorders the treatment of which is specified in the instant claims is correlated with one or more publications from the medical literature, and ultimately correlated with the activity of the compounds of the present invention.

Additionally, it should be pointed out that all of the material cited in the amendment to the specification was known by or in possession of the practitioner of ordinary skill in the art at the time the invention was made. The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. *In re* Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. *v.* Monoclonal Antibodies, Inc ., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert.* denied, 480 U.S. 947 (1987); and Lindemann Maschinenfabrik GMBH *v.* American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

When the examiner in the previous Office action invited applicants to provide evidence of the enablement of the treatment of conditions in addition to diarrhea, he did not intend to imply that all of the literature provided as evidence must be cited in the specification; it merely needed to be brought to the examiner's attention and to not have been published (or, in the case of patent literature, have a filing date) *after* the instant invention was made.

Applicant is required to cancel the new matter in the reply to this Office Action.

Allowable Subject Matter

Claims 9 and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Closest prior art with respect to instant claims 9 and 11 are the von Geldern et al 1995 reference cited supra, in the rejection of instant claim 1 under 35 U.S.C. 102, the von Geldern et al reference cited in the previous Office action, WO 97/30053 (Gordon et al), cited in the Office action mailed to applicants 5 October 2005, and another reference discovered in the updated search prior to the preparation of this Office action:

> Gordon et al, "Synthetic Approaches to the "Azole" Peptide Mimetics" Tetrahedron Letters, vol. 34(12), pages 1901-1904 (1993).

Gordon et al, on page 1904, in Table 1, reports a few imidazole compounds very similar to those according to the present invention. The only species wherein an indol-3-ylmethyl group is at the position corresponding to R^3 of formula (1), however, has a phenyl group at the position corresponding to R^5 and a methoxycarbonyl group (methyl ester group) at the position corresponding to R^6, which is not permitted in instant claim 1.

The substitution pattern specified in claims 9 and 11 is not disclosed, taught or suggested in any of these four close-prior art references.

The new matter added to the specification by virtue of the present amendment partially overcomes the provisional rejection of the now-withdrawn method of treatment claims, but not because those literature citations are incorporated into the specification, but because of what the cited references themselves teach.

Treatment of the following are still deemed to be non-enabled by the disclosure: gonadotropinoma, cancer (in general, which includes any and all cancers), cancer cachexia, hypotension (in general, which includes hypotension caused by any etiology –

postprandial hypotension is deemed enabled, however), nephropathy (which refers generally to any type of kidney pathology), "angiogenesis" (which is not properly considered to be a disorder; it is a physiological process which is part of the normal functioning of the body), "inflammatory disorders" (which includes any and all diseases or disorders that involve some type of inflammatory response – practically any disorder involving the immune system), "angioplasty" (which is a surgical procedure, not a disease), inhibiting the proliferation of *Helicobacter pylori* (the antibacterial agent in the reference cited to support this indication was not the somatostatin analog).

Should applicants amend the method claims so as to recite the *treatment of* all of the conditions *except* the ones indicated as not being enabled in the preceding paragraph, and *also* cancel claims 31-33, which are mode-of-action claims that are not enabled by virtue of the fact that the mode of action is not correlated in the claim with any specific utility or group of utilities, the withdrawn method of treatment claims would be found enabled and could be allowed upon rejoinder. If the suggested amendments to the method of treatment claims are not followed, an amendment after final which otherwise places the elected claims (drawn to compounds) in condition for allowance could be denied entry, because to rejoin the withdrawn claims would present new patentability issues under 35 U.S.C. 112 (please see MPEP 821.04(b)).

Conclusion

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX

MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 5:45am to 2:15pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Zachary C. Tucker
Primary Examiner
Art Unit 1624